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H. THOMAS ANDERTON, JR.
345 OYSTER POINT BLVD
SOUTH SAN FRANSISCO, CA 94080

| EXAMINER | |
|---|---|
| NOGUEROLA, ALEXANDER STEPHAN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1753 | |

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/726,321 | BURGI ET AL. | |
| | Examiner | Art Unit | |
| | ALEX NOGUEROLA | 1753 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 01 December 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/06/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 6, 7, 12, 13, 17, 21, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by the JPO English language computer translation of JP 11-248679 A ("Tetsuro").

Addressing claims 1 and 23, Tetsuro teaches a method of identifying one or more analytes in a sample by electrophoretic separation, the method comprising the steps of

applying a potential across a separation path containing one or more analytes to generate a current therein and to separate the one or more analytes so that a first electropherogram of a signal as a function of time is produced (paragraphs [0017], [0018], [0022], and [0023] of the Detailed Description and Drawing 2);

integrating the current with respect to time to provide a cumulative current as a function of time (paragraph [0018] of the Detailed Description and paragraph [0027] of the Example);

transforming the first electropherogram to a second electropherogram of the signal as function of the cumulative current (claim 1; formula (4) in paragraph [0011] of the Detailed Description; paragraph [0027] of the Detailed Description; and paragraph [0027] of the Example; and Drawing 4); and

identifying in the second electropherogram peaks that are correlated with the one or more analytes in the sample (paragraph [0027] of the Detailed Description and paragraph [0027] of the Example)

For claim 23 note that the claimed program is implied in Tetsuro since the electrophoresis system of Tetsuro, which includes a computer for control and data processing, performs the indicated steps, as discussed above.

Addressing claims 2 and 13, for the additional limitations of these claims see Drawing 2; paragraphs [0021]-[0026] of the Detailed Description; and paragraphs [0022]-[0026] of the Example.

Addressing claims 6 and 17, for the additional limitation of this claim see the abstract and Drawing 1.

Addressing claims 7 and 21, for the additional limitation of this claim see paragraph [0006] of the Detailed Description and paragraph [0019] of the Example.

Addressing claim 12, Tetsuro teaches a system for identifying one or more analytes in a sample using electrophoretic separation, the system comprising

separation path comprising a separation medium (Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a voltage source for applying a potential across the separation path so that a current is generated in the separation path and one or more analytes are separated along the separation path ((Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a detector positioned along the separation path for recording a first electropherogram of the signal intensity associated with the one or more analytes in the separation path as a function of time (Drawing 1 and paragraph [0006] of the Detailed Description); and

a processor comprising software for (a) integrating with respect to tie the current in the separation path to provide the cumulative current as a function of time; (b) transforming the first electropherogram to a second electropherogram of the signal intensity associated with the analytes as a function of the cumulative current; and (c) identifying in the second electropherogram peaks that are

correlated with one or more anatyes in the sample. (Drawing 1 and paragraphs [0016] to [0023]).

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 3 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Johnson et al. (US 6,372,106 B1) ('Johnson").

Addressing claim 3, Tetsuro teaches a method of identifying one or more analytes in a sample by electrophoretic separation, the method comprising the steps of

applying a potential across a separation path containing one or more analytes to generate a current therein and to separate the one or more analytes so that a first electropherogram of a signal as a function of time is produced (paragraphs [0017], [0018], [0022], and [0023] of the Detailed Description and Drawing 2);

integrating the current with respect to time to provide a cumulative current as a function of time (paragraph [0018] of the Detailed Description and paragraph [0027] of the Example);

transforming the first electropherogram to a second electropherogram of the signal as function of the cumulative current (claim 1; formula (4) in paragraph [0011] of the Detailed Description; paragraph [0027] of the Detailed Description; and paragraph [0027] of the Example; and Drawing 4); and

identifying in the second electropherogram peaks that are correlated with the one or more analytes in the sample (paragraph [0027] of the Detailed Description and paragraph [0027] of the Example)

Tetsuro does not mention varying the potential with time, although Tetsuro does disclose performing electrophoresis at different, albeit fixed, potentials See Drawing 2.

Johnson discloses varying voltage while performing capillary electrophoresis. See the abstract. it would have been obvious to one with ordinary skill in the art at the time of the invention to vary the voltage as taught by Johnson in the invention of Tetsuro because as taught by Johnson this will reduce peak broadening. See in Johnson the abstract; col. 1:5-14; and col. 2:17-20. As for having the second electropherogram be a function further comprised of the potential as a function of time, in light of Drawing 2 of Tetsuro, for example, which discloses generating electropherograms at several different voltages, electropherograms using several different voltage programs would also be tried.

Addressing claim 14, Tetsuro teaches a system for identifying one or more analytes in a sample using electrophoretic separation, the system comprising

separation path comprising a separation medium (Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a voltage source for applying a potential across the separation path so that a current is generated in the separation path and one or more analytes are separated along the separation path ((Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a detector positioned along the separation path for recording a first electropherogram of the signal intensity associated with the one or more analytes in the separation path as a function of time (Drawing 1 and paragraph [0006] of the Detailed Description); and

a processor comprising software for (a) integrating with respect to tie the current in the separation path to provide the cumulative current as a function of time; (b) transforming the first electropherogram to a second electropherogram of the signal intensity associated with the analytes as a function of the cumulative current; and (c) identifying in the second electropherogram peaks that are correlated with one or more anatyes in the sample. (Drawing 1 and paragraphs [0016] to [0023]).

Tetsuro does not mention varying the voltage with time, although Tetsuro does disclose performing electrophoresis at different, albeit fixed, potentials See Drawing 2.

Johnson discloses varying voltage while performing capillary electrophoresis. See the abstract. it would have been obvious to one with ordinary skill in the art at the time of the invention to vary the voltage as taught by Johnson in the invention of Tetsuro because as taught by Johnson this will reduce peak broadening. See in Johnson the abstract; col. 1:5-14; and

col. 2:17-20. As for having the second electropherogram be a function further comprised of the potential as a function of time, in light of Drawing 2 of Tetsuro, for example, which discloses generating electropherograms at several different voltages, electropherograms using several different voltage programs would also be tried.

7. Claims 4 and 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Johnson et al. (US 6,372,106 B1) ('Johnson") as applied to claims 3 and 14 above, and further in view of Kuroso et al. ("Comparison of the reproducibility in migration times between a constant-current and a constant-voltage mode of operation in capillary zone electrophoresis," Journal of Chromatography A, 802 (1998) 391-394) ("Kurosu").

Tetsuro as modified by Johnson does not discloses having the potential vary with time such that the current in the separation path is constant, although it should be noted that Tetsuro does disclose constant current at constant electrophoresis voltage (Drawing 3) and Johnson discloses monitoring the electrophoresis current through the separation path and adjusting the electric field in response to the current measurement (col. 9:28-40).

Kurosu compared the reproducibility in migration times between a constant-current and a constant-voltage mode of operation in capillary zone

electrophoresis. See the title and abstract. It would have been obvious to one with ordinary skill in the art at the time of the invention to have the current be constant because as taught by Kurosu, "We found that the CC [constant-current] mode gave a better reproducibility than the CV mode in both successive injections (5 or 6 times) and day-to-day analyses (16 measurements throughout 4 days)." See the abstract.

8. Claims 5 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Johnson et al. (US 6,372,106 B1) ('Johnson") as applied to claims 3 and 14 above, and further in view of the CAPLUS abstract of Schaffer et al. ("Constant (optimum) power electrophoresis," Analytical biochemistry (1973), 51(2), 577-83) ("Schafer").

Tetsuro as modified by Johnson does not mention using a constant power supply.

Schaffer and Williams both teach using a constant power supply for electrophoresis. It would have been obvious to one with ordinary skill in the art at the time of the invention to use a constant power supply as taught by Schaffer or Williams in the invention of Tetsuro as modified by Johnson because as taught by Schaffer a constant power supply is optimum "with respect to the ratio of

migration velocity to heating, [and] produces the maximum voltage gradient consistent with the maximum allowable rate of heating."

9. Claims 8 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over the JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Chan (US 5,139,630) ("Chan")

Addressing claim 8, Tetsuro teaches a method of identifying one or more analytes in a sample by electrophoretic separation, the method comprising the steps of

applying a potential across a separation path containing one or more analytes to generate a current therein and to separate the one or more analytes so that a first electropherogram of a signal as a function of time is produced (paragraphs [0017], [0018], [0022], and [0023] of the Detailed Description and Drawing 2);

integrating the current with respect to time to provide a cumulative current as a function of time (paragraph [0018] of the Detailed Description and paragraph [0027] of the Example);

transforming the first electropherogram to a second electropherogram of the signal as function of the cumulative current (claim 1; formula (4) in paragraph [0011] of the Detailed Description; paragraph [0027] of the Detailed Description; and paragraph [0027] of the Example; and Drawing 4); and

identifying in the second electropherogram peaks that are correlated with the one or more analytes in the sample (paragraph [0027] of the Detailed Description and paragraph [0027] of the Example)

Tetsuro also teaches using at least one electrophoretic mobility standard in the sample, wherein the at least one electrophoresis standard is used to identify peaks that are correlated with the one or more analytes of the sample. See paragraph [0006] of the Detailed Description and paragraph [0019] of the Example.

Chan teaches a capillary electrophoresis method comprising two electrophoretic standards wherein the mobility of the first electrophoretic standard is greater than that of any analyte and the mobility of the second electrophoretic standard is less than that of any analyte in the sample. See the abstract and col. 3:24 – col. 4:24. It would have been obvious to one with ordinary skill in the art at the time of the invention to use two electrophoretic standards as taught by Chan in the invention of Tetsuro because as taught by Chan then sample constituents in different samples fro the same source can be identified "without resort to visual identification guesswork or concern as to changes in sample which will affect the retention time of the sample constituents." See col. 3:13-33.

Addressing claim 22, Tetsuro teaches a method of identifying one or more analytes in a sample by electrophoretic separation, the method comprising the steps of

applying a potential across a separation path containing one or more analytes to generate a current therein and to separate the one or more analytes so that a first electropherogram of a signal as a function of time is produced (paragraphs [0017], [0018], [0022], and [0023] of the Detailed Description and Drawing 2);

integrating the current with respect to time to provide a cumulative current as a function of time (paragraph [0018] of the Detailed Description and paragraph [0027] of the Example);

transforming the first electropherogram to a second electropherogram of the signal as function of the cumulative current (claim 1; formula (4) in paragraph [0011] of the Detailed Description; paragraph [0027] of the Detailed Description; and paragraph [0027] of the Example; and Drawing 4); and

identifying in the second electropherogram peaks that are correlated with the one or more analytes in the sample (paragraph [0027] of the Detailed Description and paragraph [0027] of the Example)

Tetsuro also teaches using at least one electrophoretic mobility standard in the sample, wherein the at least one electrophoresis standard is used to identify peaks that are correlated with the one or more analytes of the sample. See paragraph [0006] of the Detailed Description and paragraph [0019] of the Example.

Chan teaches a capillary electrophoresis method comprising two electrophoretic standards wherein the mobility of the first electrophoretic standard is greater than that of any analyte and the mobility of the second

electrophoretic standard is less than that of any analyte in the sample. See the abstract and col. 3:24 – col. 4:24. It would have been obvious to one with ordinary skill in the art at the time of the invention to use two electrophoretic standards as taught by Chan in the invention of Tetsuro because as taught by Chan then sample constituents in different samples fro the same source can be identified "without resort to visual identification guesswork or concern as to changes in sample which will affect the retention time of the sample constituents." See col. 3:13-33.

10. Claims 9-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Chan (US 5,139,630) ("Chan") as applied to claims 8 and 22 above, and further in view of Matray et al. (US 6,673,550 B2) ("Matray').

Addressing claim 9, Tetsuro as modified by Chan does not mention having the analytes be molecular tags, wherein each tag has a different electrophoretic mobility.

Matray teaches electrophoresis tag reagents comprising fluorescent compounds. "In one embodiment, detection involves the release of identifying tags as a consequence of target recognition. Target antilingands are contacted with a set of e-tag probes and the contacted antiligands are treated with a

selected cleaving agent resulting in a mixture of e-tag reporters. Typically, uncleaved or partially cleaved e-tag probes are removed and the mixture of e-tag reporters is separated by any technique that provides for separation by mass or mass to charge ration and the like and detected to provide for target identification." See the abstract. Matray further teaches, "By using protocols that result in the release of eTag™ reporters from the binding compound that are identifiable due to differences in mobility, the analysis is greatly simplified, ..." See col. 4:59-67. It would have been obvious to one with ordinary skill in the art at the time of the invention to use tags as taught by Matray in the invention of Tetsuro as modified by Chan because as taught by Matray multiple analytes in a sample may be simultaneously determined. See col. 3:12-26.

Addressing claim 10, for the additional limitation of this claim note that Matray teaches, "The present compositions may be employed in the detection and quantitation of analytes such as polypeptides, polyucleotides, hormones and drugs" and "Methods and compounds are provide for multiplexed determinations, where the compounds can be linked to binding compounds for detection of reciprocal binding compounds in a sample." See col. 1:18-22 and col. 3:63-66

Addressing claim 11, as for using from 2 to 50 molecular tags, the number of tags will depend on the number of analytes of interest. So if 2 to 50 analytes are of interest from 2 to 50 tags will be used.

11. Claims 18/12, 19/18/12, and 20/18/12 are rejected under 35 U.S.C. 103(a) as being unpatentable over the JPO English language computer translation of JP 11-248679 A ("Tetsuro") in view of Mathies et al. (US 5,274,240) ('Mathies').

Tetsuro teaches a system for identifying one or more analytes in a sample using electrophoretic separation, the system comprising

separation path comprising a separation medium (Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a voltage source for applying a potential across the separation path so that a current is generated in the separation path and one or more analytes are separated along the separation path ((Drawing 1 and paragraphs [0003] and [0006] of the Detailed Description);

a detector positioned along the separation path for recording a first electropherogram of the signal intensity associated with the one or more analytes in the separation path as a function of time (Drawing 1 and paragraph [0006] of the Detailed Description); and

a processor comprising software for (a) integrating with respect to tie the current in the separation path to provide the cumulative current as a function of time; (b) transforming the first electropherogram to a second electropherogram of the signal intensity associated with the analytes as a function of the cumulative current; and (c) identifying in the second electropherogram peaks that are correlated with one or more anatyes in the sample. (Drawing 1 and paragraphs [0016] to [0023]).

Tetsuro does not mention providing a plurality of separation paths. As a

first matter, baring a contrary showing, such as unexpected results, this limitation is just multiplication of parts for a multiplied effect; that is so that a plurality of electrophoresis separations can be simultaneously performed. In any event, Mathies teaches providing a plurality of capillaries in an electrophoresis system. See the abstract. It would have been obvious to one with ordinary skill in the art at the time of the invention to provide a plurality of capillaries as taught by Mathies in the invention of Tetsuro because as taught by Mathies not only can a plurality of samples be run simultaneously, "... individual capillaries can be independently manipulated at the inlet, thereby facilitating rapid, parallel loading of multiple samples. In our approach, the capillaries are combined into a ribbon at the outlet for ease of parallel, on-column detection. In this way, a two order-of-magnitude increase in CE throughput should be achieved because hundreds of capillaries can be easily bundled for detection." See col. 1:68 – col. 2:7.

For claims 19 and 20 note that whether an independent potential is applied across each separation path or a potential is jointly applied across the separation paths will just depend on samples and samples and purpose of the runs. For example, it would have been obvious to jointly apply a potential across the separation paths if the samples in each separation path are the same; that is, if they are replicates run for statistical purposes. On the other hand, if the samples are significanlty different such as proteins in one separation path, nucleic acids in another, and so on, it would have been obvious to use a different potential across each path to optimize the different sepaations

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
February 3, 2006